Nitric Oxide and Prostaglandin E2 Participate in Lipopolysaccharide/Interferon g Induced Heme Oxygenase 1 And Prevent RAW264.7 Macrophages from UV-Irradiation Induced Cell Death.

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Abstract

Induction of heme oxygenase (HO)-1 during inflammation has been demonstrated in many cell types, but the contribution of inflammatory molecules nitric oxide (NO) and prostaglandin E2 (PGE2) has remained unresolved. Here we show that NO donors including sodium nitroprusside (SNP) and spermine nonoate (SP-NO), and PGE2 significantly stimulate HO-1 expression in RAW264.7 macrophages, associated with alternative induction on NO and PGE2 in medium, respectively. NO donors also show the inductive effect on cyclo-oxygenase 2 protein and PGE2 production. In the presence of lipopolysaccharide and interferon- (LPS/IFN-), HO-1 protein was induced slightly but significantly, and SNP, SP-NO, and PGE2 enhanced HO-1 protein induced by LPS/IFN-. L-Arginine analogs N-nitro-L-arginine methyl ester (L-NAME) and N-nitro-L-arginine (NLA) significantly block HO-1 protein induced by LPS/IFN- associated with a decrease in NO (not PGE2) production. And, NSAIDs aspirin and diclofenase dose dependently inhibited LPS/IFN--induced HO-1 protein accompanied by suppression of PGE2 (not NO) production. PD98059 (a specific inhibitor of MEKK), but not SB203580 (a specific inhibitor of p38 kinase), attenuated PGE2 (not SP-NO) induced HO-1 protein. Under UVC (100 J/m2) and UVB (50 J/m2) irradiation, PGE2 or SP-NO treatment prevents cells from UVC or UVB-induced cell death, and HO-1 inhibitor tin protoporphyrin (SnPP) reverses the preventive effects of PGE2 and SP-NO. The protective activity induced by PGE2 on UVC or UVB irradiation-induced cell death was blocked by MAPK inhibitor PD98059 (not SB203580). These results demonstrated that inflammatory molecules NO and PGE2 were potent inducers of HO-1 gene, and protected cells from UV-irradiation-induced cell death through HO-1 induction. J. Cell. Biochem. 86: 331-339, 2002.